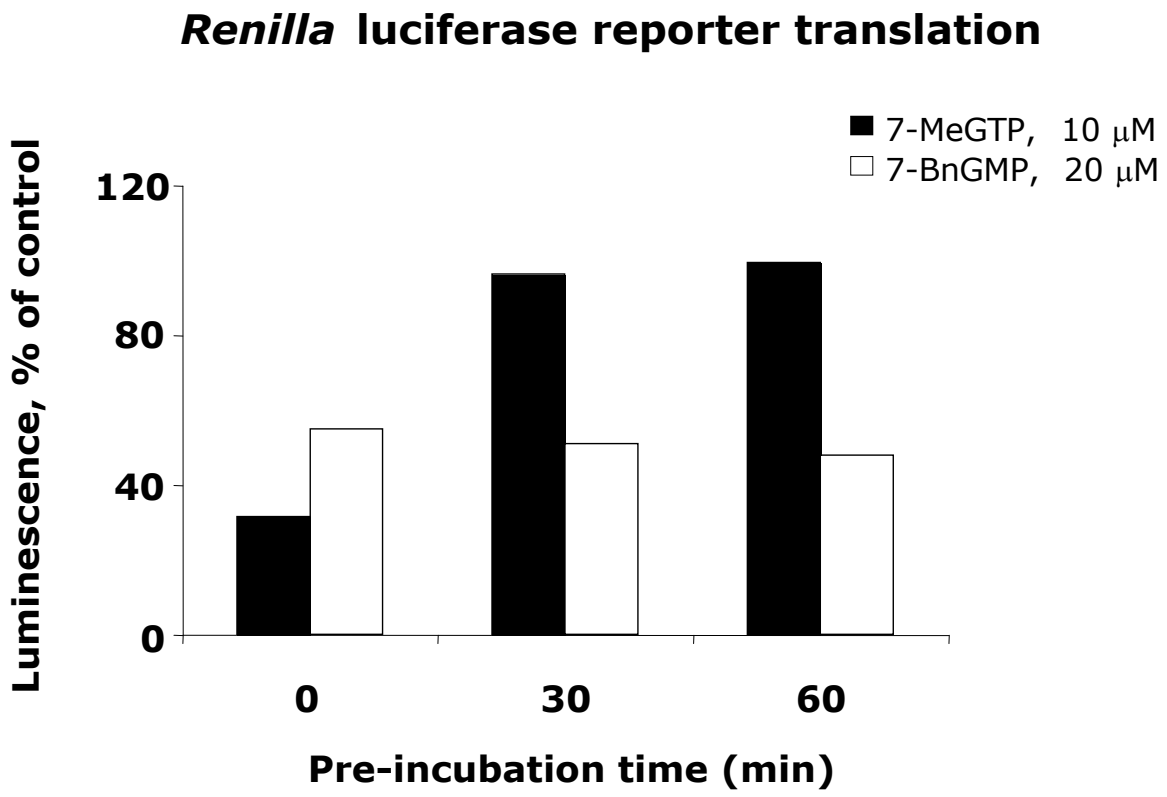
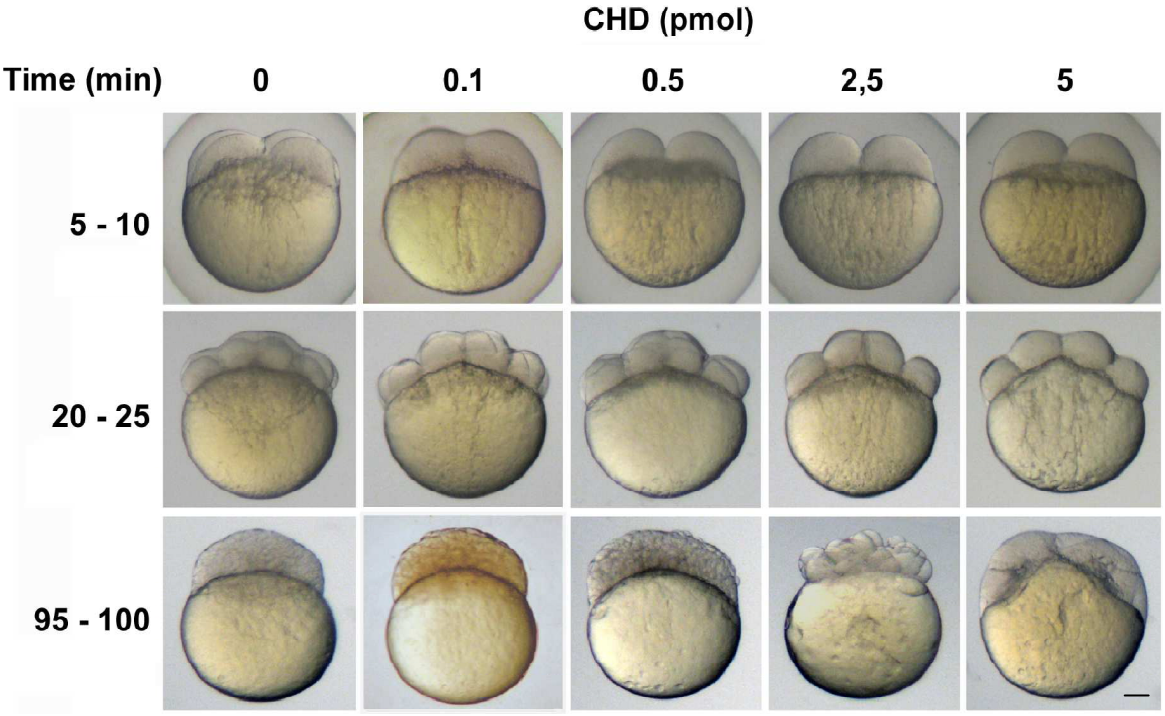
Supplementary Figure 1



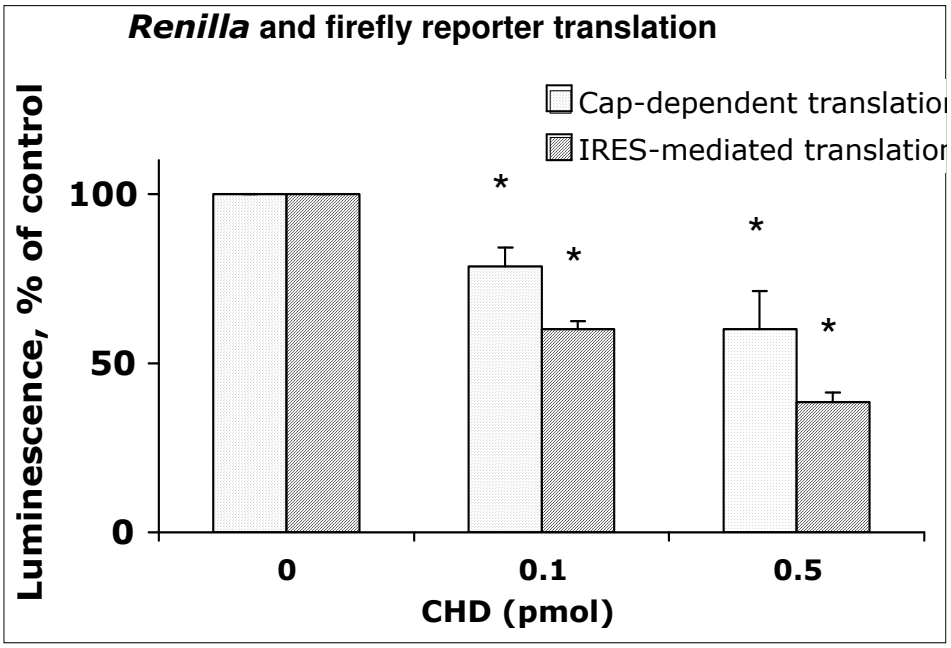
Supplementary Figure 2

A

B



C



Supplementary Figure 3

213-217 aa

Supplementary Table 1. Experimental Details: Explant[#] morphology and PCR analysis

Injected:	Time in culture, h	Number of explants	Elongated explants (%)	Marker expression			
				ntl	*myoD*	*cytI*	*gta3*
4E WT	**1**	**201***	**0**	-	-	+	+
	24	**124***	**79**	+	+	+	+
	48	**56**	**80‡**	ND			
4E WT+4Ei1	**1**	**106***	**0**	-	-	+	+
	24	**101***	**0**	-	-	+	+
	48	**24**	**0**	ND			
xEF1-α	**1**	**192***	**0**	-	-	+	+
	24	**112***	**0**	-	-	+	+
	48	**35**	**0**	ND			
4E W56A	**1**	**160***	**0**	-	-	+	+
	24	**190***	**0**	-	-	+	+
	48	**40**	**0**	ND			
Buffer (HBSS)	**1**	**61**	**0**	-	-	+	+
	24	**61**	**0**	-	-	+	+
	48	**18**	**0**	ND			
4E WT+7-BnGMP	**3**	**34**	**0**	ND			
	48	**31**	**0**	ND			

[#]Explants were generated as outlined in **Figure 5** and **METHODS**.

*****Explants were harvested after 1 and 24 hours in culture. In all experimental and control series, total RNA extraction was performed independently from 2 groups containing 48 to 70 explants. RT-PCR analysis was performed for each RNA preparation (independently replicated).

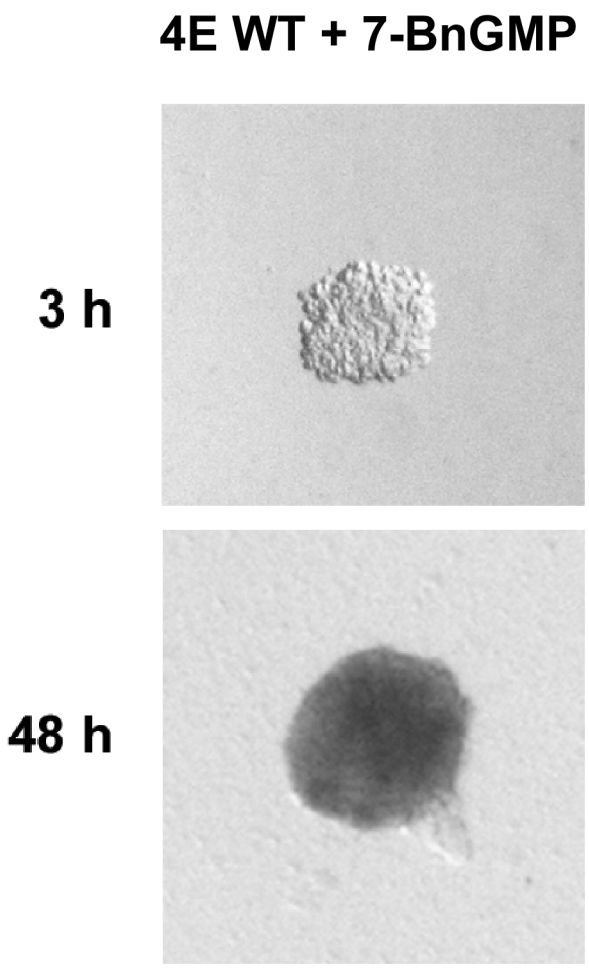
+ indicates positive results in all runs

- indicates negative results in all runs

ND indicates not done (explants too fragile to collect and prepare intact RNA)

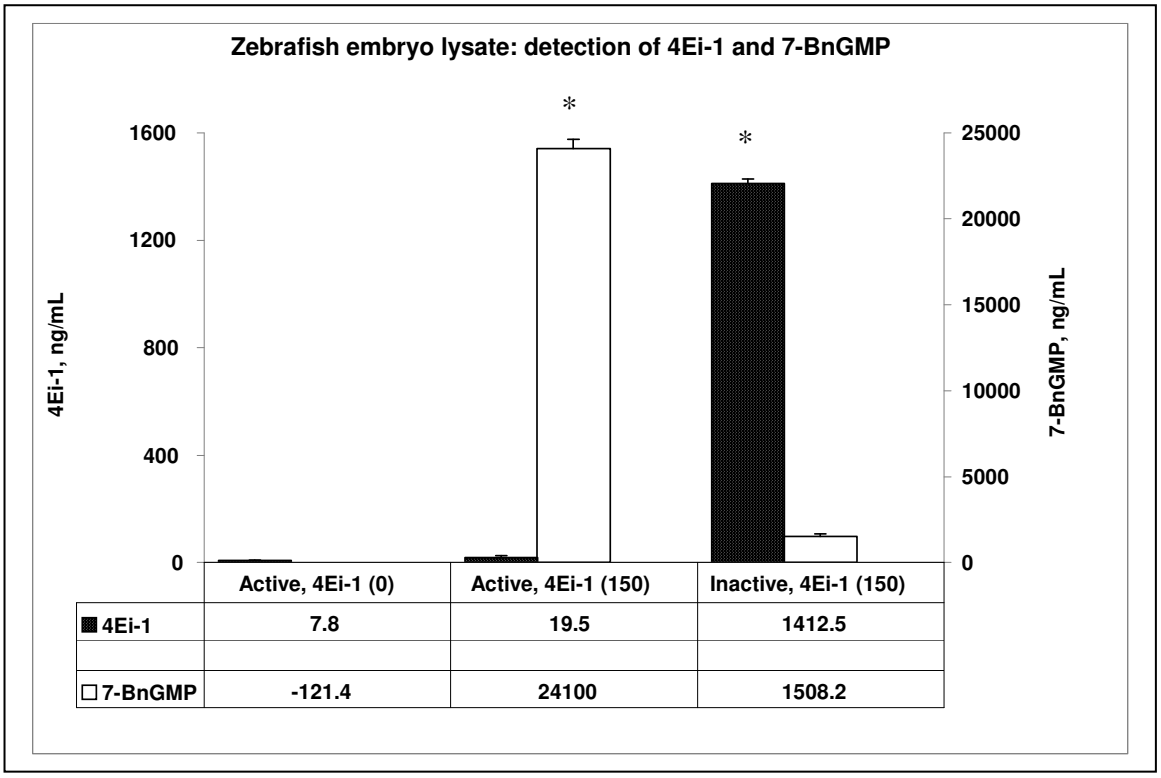
‡ indicates elongated explants with motile cells

Supplementary Figure 4



Supplementary Figure 5

A



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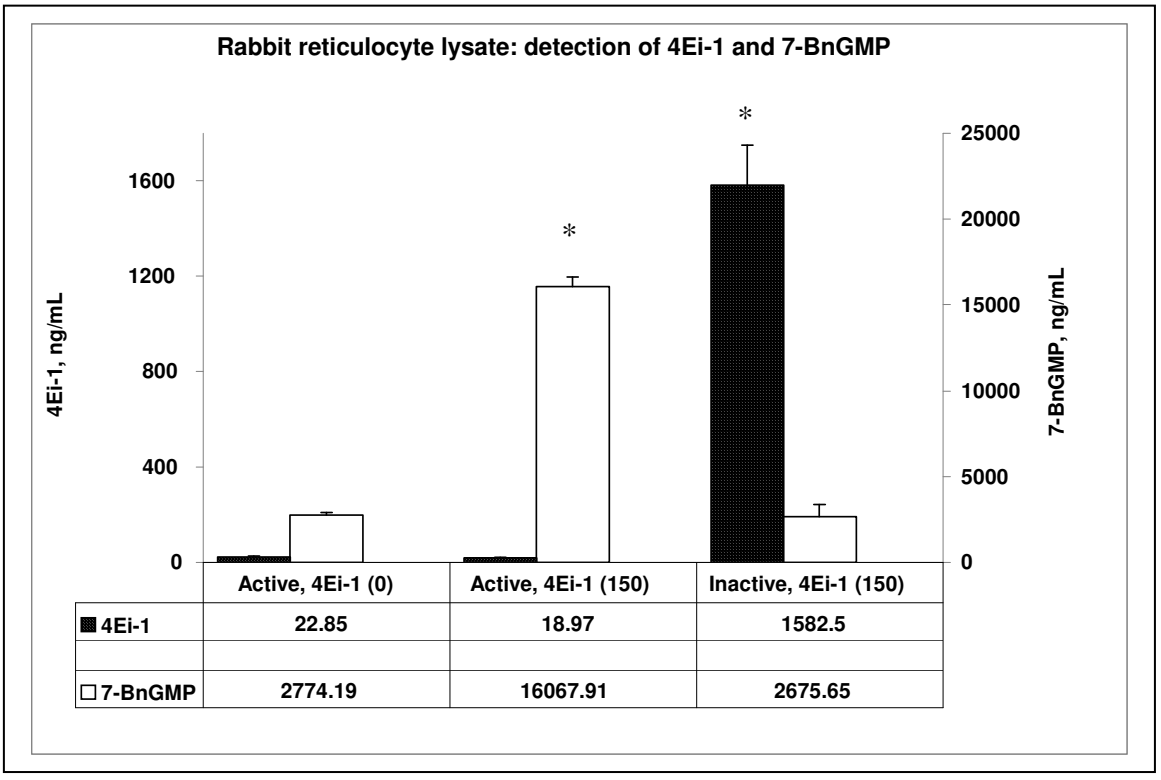

Supplementary Figure legends:

Supplementary Figure 1. Stability of 7-BnGMP in a biological milieu *in vitro*. *7-Bn GMP (20 μM) and 7-Me GTP (10 μM) were pre-incubated in* Rabbit reticulocyte lysate for 0, 30 or 60 min prior to the start of *in vitro* translation. *Renilla* luciferase reporter was quantified as a measure of cap-dependent translation. Shown is a representative histogram of *Renilla* reporter luminescence (arbitrary units) with all values normalized to luminescence in a compound-free control reaction. Compounds are tested at concentrations that account for the difference in the IC_{50} values.

Supplementary Figure 2. Validation and calibration of the Zebrafish Translation Assay using cycloheximide (CHD).

A) Map of the *in vitro*-generated dual-luciferase reporter mRNA. Reporter was microinjected into single-stage eggs; cycloheximide (dose range, 0.1 to 5 pmol), which suppresses polypeptide elongation by inhibiting 60S ribosomal peptidyl transferase – thus inhibiting both cap-dependent and IRES mediated reporter translation – was injected at the 2-cell stage. Eggs and embryos were observed at cleavage, gastrulation, somitogenesis and hatching; whole embryo lysates taken at the late blastula stage was analyzed for luminescence as a measure of cap-dependent translation. Shown are the map and structure of the reporter mRNA.

B) Morphology. Impact of CHD on cell division and development. Shown are eggs (lateral view) after CHD exposure for the times indicated, observed in 3 independent experiments (scale bar, 250 μm).

C) Translation. Shown is the impact of CHD on reporter translation with all values normalized to the luminescence of embryos injected with buffer only (left bar). Data are presented as mean ±

SEM for 3 independent experiments conducted with 20 embryos each; * indicates a significant difference at $p < 0.01$ compared to the buffer calibration control set at 100.

Supplementary Figure 3. eIF4E is highly conserved across vertebrate species. Multiple alignment of the protein sequences of zebrafish, *Xenopus*, mouse and human eIF4E deposited in the SwissProt database were compared using the T-COFFEE software, version 2.88. Computation was performed at the Swiss Institute of Bioinformatics using the Blast network service. Residues in red are identical in all the aligned sequences. Residues in orange are also identical in the zebrafish and murine sequences. Asterisks in green (with arrows) demarcate the "core" eIF4G-binding region; residues in blue indicate the point mutation site used in our experiments (amino acid 56 in the human protein sequence) in which W is substituted for A impairing the ability of eIF4E to bind cap *(61)*. As previously reported *(62)*, zebrafish and mouse eIF4E 1A isoforms share 83% overall similarity and almost 90% identity at the "core" eIF4G-binding site.

Supplementary Figure 4. 7-BnGMP suppresses EMT in ectodermal zebrafish explants. eIF4E WT mRNA (2 ng) and 7-BnGMP (25 pmol) were co-injected into zebrafish fertilized eggs at the one-cell stage. Ectoderm blastula explants were excised prior to germ layer restriction and cultured individually. Shown is explant morphology at 3 and 48 h post excision. Within 3h, explants changed their shape from rectangular to spheroid. By 48 h, neither explant elongation, nor motile cells was observed indicating the absence of EMT.

Supplementary Figure 5. Conversion of 4Ei-1 to 7-BnGMP in cell lysates. Concentrations of **4Ei-1** and the corresponding monophosphate, 7-BnGMP were quantified by mass spectrometry as a measure of **4Ei-1** processing. Lysates (active and heat-inactivated) were incubated for 1 h at 30^{o}C with **4Ei-1** at a final concentration of 150 μM [**4Ei-1** (150)] and without **4Ei-1** [**4Ei-1** (0)].

A) Detection of 4Ei-1 and 7-BnGMP in zebrafish embryo lysate.

B) Detection of 4Ei-1 and 7-BnGMP in rabbit reticulocyte lysate.

Shown are histograms representing concentration values (ng/mL) of **4Ei-1** and 7-BnGMP in lysates (17 μL) after 1h of incubation at 30°C. Data are presented as mean ± SEM for 2 independent experiments; * indicates a significant difference at $p < 0.001$ compared to the compound-free control.